CLINICAL SURVEILLANCE OF FEBRILE PATIENTS AND INCIDENCE OF SALMONELLA TYPHI IN OUAGADOUGOU, BURKINA FASO

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CLINICAL SURVEILLANCE OF FEBRILE PATIENTS AND INCIDENCE OF SALMONELLA TYPHI IN OUAGADOUGOU, BURKINA FASO

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List of Abbreviations

AIR	Adjusted incidence rates
AMR	Antimicrobial resistance
CNS	Coagulase Negative Staphylococci
E Coli	Escherichia Coli
GBD	Global Burden of Disease
HDSS	Health and Demographic Surveillance System
IVI	International Vaccine Institute
KOICA	Korea International Cooperation Agency
LMIC	Low- and Middle-Income Countries
MDR	Multi-drug resistance
NTS	Non Typhoidal Salmonella
PYO	Person-years of Observation
S. Typhi	Salmonella Typhi
TF	Typhoid Fever
WASH	Water Sanitation and Hygiene

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Abstract

Typhoid fever (TF) is an acute gastrointestinal infection caused by the bacterium Salmonella enterica serotype Typhi (S. Typhi), which is transmitted through contaminated food or drinking water from one person to another. Salmonella bacteria is one of the leading causes of community-acquired bloodstream infection which record a high mortality rate in sub Saharan Africa. High incidence of TF is particularly observed in low income countries in sub-Saharan Africa.

The objective of this study is to estimate the incidence of TF in Ouagadougou Burkina Faso. Two regions within the capital city Ouagadougou, Nioko and Polesgo, were selected to carry out a population-based prospective febrile surveillance which took place between 2015 and 2016.

Participants residing in these two areas and who presented with acute fever ≥38˚C, using tympanic temperature records were enrolled into the study. Participants with a history of fever more than 72 hours and <38˚C and those leaving out of catchment area were excluded from the study. Blood samples were collected from participants and a blood culture was conducted to confirm bacteremia. The results of 1,306 blood culture conducted confirmed 21 samples positive for Salmonella bacteria between 16 June 2015 and 25 April 2016 of which 9 were S. Typhi infections.

Two cases were found in children less than 5 years old three cases in the group between 6-15 years. The incidence of S. Typhi overall was calculated to be 125 per 100,000 person years of observation (PYO) with highest prevalence seen in children <5 years.

The prevalence of Multi- drug resistant (MDR) S. Typhi isolates, defined as resistance to three or more classes of antibiotics, was high (7/9).

Administration of an effective typhoid fever vaccine in children under 5 years of age may be an effective strategy to reduce the burden of TF in Burkina Faso. Further studies characterizing the severity of S. Typhi infections, including the development of intestinal perforation and mortality and including rural areas are necessary.

Chapter I:

1.1. Introduction

Typhoid fever (TF) is an acute gastrointestinal infection caused by the bacterium Salmonella enterica serotype Typhi (S. Typhi), which is transmitted through the fecal-oral route with contaminated food or drinking water from a sick person or healthy carrier to another person. (Park, 2015) (Baker, Hombach, & Marks, 2016)(Steele et al., 2016) TF is characterized by an onset of high fever, extreme fatigue, headache, constipation, chills, and muscle pain. Other symptoms include: an enlarged liver, lack of appetite, and some patients may present with diarrhea and vomiting, a rash on their trunk.(Steele et al., 2016) Symptoms of TF can be noticed 1 to 3 weeks after exposure to the S. Typhi bacteria, and severe symptoms such as confusion, intestinal hemorrhage, perforation, delirium, may be noticed 2 to 3 weeks after onset of the illness based on bacteria multiplication in the intestinal tract of the affected individual.(Andrade & Andrade, 2016)

TF remains a significant contributor to global mortality and morbidity which is a leading cause of community-acquired bloodstream infection in sub Saharan Africa. A recent estimate of global incidence is in between 11 million and 18 million cases annually, with a mortality rate estimated between 128,000 and 190,200 deaths per year. (Crump & Chb, 2017) The incidence of TF in sub Saharan African is 100 per 100,000 PYO with 33,490 deaths about 26.0% of global Typhoid deaths. (Mogasale et al., n.d.) (Crump & Heyderman, 2019)

The incidence of TF in Burkina Faso remains very high with 383 per 100,000 PYO. (Marks et al., 2017)

In most Low and middle income countries (LMIC) little or no surveillance programs and information on incidence and burden of the TF exist so there is high need to carry out studies in sub Saharan Africa such as Burkina Faso. (Baker et al., 2016)

Burkina Faso is a country in West Africa sharing boundaries with Mali in the north, Ghana and Togo in the south, Ivory Coast in the southwest, Niger in the east and Benin in the southeast. Burkina Faso has a land surface that covers an area of about 274,200 square kilometers. The capital city is Ouagadougou and their official language is French but there are over 70 languages spoken.

Doing a study on clinical surveillance of febrile patients and incidence of S. Typhi in the catchment area will provide information on the burden of disease to the health policy makers to act by introducing a TF mass vaccination campaign or by improving on Water, sanitation and hygiene (**WASH)** in the affected areas. The administration of TF vaccine in the catchment area of Ouagadougou will immunize the population against invasive S. typhi which will greatly reduce the number of TF cases that will occur through transmission from person to person. The drop in TF cases in the community will reduce the number of sick persons thereby reducing the prevalence of premedication at home by the population. (Marks et al., 2017) Premedication is common in Africa due to the fast-growing rate of over-the-counter drugs which are cheaper. This drop in the number of TF cases will equally reflect on the fall in the prevalence of MDR due to abusive use of antibiotics at home and misused in hospitals because of poor diagnosis.

1.2. Goal

The goal of this study is to determine the burden of S. Typhi infection in the catchment area of Nioko and Polesgo in Ouagadougou, Burkina Faso.

1.3. Objectives

We will determine the incidence of TF and characterized the population at risk in the catchment area. The prevalence of MDR to first line antibiotics will be measured and assess the frequently used antibiotics or analgesics by participants as premedication before visiting health care unit.

LITERATURE REVIEW

2.1. Review on burden of the disease

Global Burden of typhoid and paratyphoid fever morbidity is estimated at 15.5 million with about 154,000 deaths in 2016.(Marks et al., 2017) Another TF estimated incidence in west Africa is about 10–100 cases per 100,000 person-years of observation (PYO) that occurs mostly in urban areas with high population densities(Marks et al., 2017)(Bill & Foundation, 2017).

Estimated global incidence of 14·3 million cases of typhoid and paratyphoid fevers occurred in 2017 giving a 44·6% drop from 25·9 million cases in 1990. 76·3% of enteric fever was caused by S. Typhi with a global case fatality estimated at about 0·95% in 2017. This case fatality was higher among children than older adults living in lower-income countries. (Bill & Foundation, 2017) A recent estimate of global incidence TF is between 11 million and 18 million cases annually, with a mortality rate estimated between 128,000 and 190,200 deaths per year. (Crump & Chb, 2017)

Incidence rate from confirmed invasive Salmonella infections were estimated using Adjusted incidence rates (AIRs) per 100,000 PYO in the catchment population. Calculated PYO in catchment area was by projecting the study population from the start to the end of recruitment period using annual growth rates of the country. (Kalckreuth et al., 2016)

Adjusted incidence rates (IRs) were estimated from confirmed invasive Salmonella infections in catchment populations per 100,000 person-years of observation (PYO) and from incidences of previously published documents. All resident patients in the catchment area contributed to PYO and their contribution ended when the person no longer stay or died during the surveillance period for HDSS sites. The annual population growth rate of the country was used to calculated PYO by projecting the population of the catchment area from the beginning to the end of the study period. (Kalckreuth et al., 2016)

MDR S. Typhi isolated is an increasing problem in the world especially in south and southeast Asia for decades with H58 strain which is migrating to African countries. (Marks et al., 2017) This strain might cause TF in previously absent geographical areas and such strains might stimulate the use of antibiotics to increased where it is bought over the counter or available without any prescription because S. Typhi respond more slowly to antibiotic treatment. (Kalckreuth et al., 2016)

2.2. Review on antimicrobial resistance to antibiotics

MDR strains will increase TF disease burden in LMIC due to the lack of high-quality diagnostic equipment and misuse of antimicrobial drugs. This scale of antimicrobial resistance is a problem that will gradually grow as years pass by and this has been observed in sub Saharan Africa (Baker et al., 2016).(Fever & Overview, 2011). Given the widespread use of antimicrobials in sub-Saharan Africa, additional data from Ouagadougou, Burkina Faso, which has good laboratory-based diagnostic capacity for detecting bacterial antibiotic resistance from previous studies is important.

2.3. Review on diagnosis of typhoid fever

Limitations in diagnosis in most rural areas with poor water quality, hygiene and sanitation (**WASH**), restricted access to medical care, overcrowding, will be a problem in assessing the burden of invasive Salmonella disease. This inability to diagnose patients in those areas will underestimate the burden of invasive Salmonella disease and increasing incidence of the disease. (Baker et al., 2016)

The incidence of TF in many parts of Africa has been underestimate due to difficulties in microbial culture of the disease leading to substantial disease burden. (Dougan, n.d.)

Many countries are still uncertain with the true disease burden for S. Typhi infection due to little or no surveillance or systematic hospital-based surveillance. This bad situation is worsen with the lack of accurate rapid diagnostic kits, poor disease reporting systems, no frequent laboratory testing, and clinical diagnosis of typhoid is often difficult due the occurrence of more than one febrile illness in the same patient such as dengue or malaria fever.(Steele et al., 2016)

2.4. Review on control and prevention of typhoid fever

Many multilateral donors have developed a better and easier to use diagnostic tests without the use of cumbersome techniques to diagnose typhoid in rural area and the test can be performed at any point in time. They also introduce preventive vaccination against S. Typhi infections to targeted remote areas in order to reduce the disease burden (Steele et al., 2016). This move will facilitate the diagnosis of TF in rural areas where TF is endemic for effective management and prevention of disease spread to other persons. The effectiveness of TF vaccine usage is one of the preventive measures against invasive Salmonella disease in high risk zones which must be implemented by policymakers to reduce the incidence that affects mostly the younger age groups in rural areas with low population density. (Marks et al., 2017)

Studies have shown that good knowledge, attitude and practice of **WASH** such as washing of hands after visiting the toilet, wash fruits before eating, drink good water and mass vaccination with the new TF conjugate vaccine will reduce the burden of the invasive Salmonella disease thereby reducing the incidence of MDR.(Al-emran et al., 2016) Contaminants organisms included non-pathogens like bacteria, fungi, Coagulase- negative Staphylococci (CNS), Hey Bacillus, which are not associated with bloodstream infections but commonly associated with skin microbiota may mask the S. Typhi. (Marks et al., 2017)

Invasive Salmonella disease is one of African agenda top public health priority disease which will be eliminated with the development of typhoid fever conjugate vaccines and its administration to the endemic area of high incidence of typhoid fever. The TF community needs to tackle the political issues surrounding TF immunization now if they believe that regional elimination of S. Typhi is a tangible target. (Baker et al., 2016)(Article, 2016)

The introduction of S. Typhi infection vaccine in to the immunization calendar of children under 5 years of age will have a greater effect in reducing the disease incidence in children under the age of 5 years particularly in children less than 2 years who are affected more with the S. Typhi infections (Balasubramanian et al., 2018)

METHODS

3.1. Study site

This study was carried out within the Nioko and Polesgo health areas in the north of Ouagadougou Burkina Faso. The site was included in this study because of evidence from previous TF reports in the surveillance conducted by the Typhoid Fever Surveillance in Africa Program (TSAP), laboratory infrastructure suitable for blood culture with experience microbiological laboratory staff, and access to a functional health and demographic surveillance system (HDSS) in the target area.

3.2. Study Design

This is a population-based prospective febrile surveillance using data between 16 June 2015 to 25 April 2016 of Kossodo Health Center a public health unit which serve patients of all ages in Nioko and polesgo health area of north Ouagadougou Burkina Faso. Blood culture test in combination with malaria parasite test was also done using a rapid diagnostic test with the blood sample in order to have a differential diagnosis.

3.3. Study population

Recruitment was opened to all 28,701 inhabitants of the catchment area but a the section criterial was made such as any person with high temperature ≥38.0°C, visiting the Kossodo health center during the study period from 16 June 2015 to 25 April 2016 and were staying in the catchment area were enrolled into the study, and those with a history of fever more than 72 hours and <38˚C, as well as patient resident out of catchment area were excluded from the study (Mark et al.,2017).

3.4. Sample size

Blood samples were collected from 1,306 persons who made the enrollment criterial and a blood culture test was performed for each person.

Statistical analysis

Isolation test for MDR was done to know the prevalence of drug resistance within S. typhi bacteria in the catchment area. Participants consent were obtained for eligible participants before enrollment and collection of blood samples.

Data was obtained and the results were analyzed in tables and figures, these results were used to estimate the incidence of typhoid fever in the Burkina Faso. The incidence of S. Typhi also known as rate is been calculated by the total number of new cases of TF (numerator) divided by the population at risk (denominator) from the beginning of the observation period usually for a year and the unite express per 100,000 person per year of observation. (Dvm, 2017)

$$\text{Incidence rate} = \frac{\text{the total number of new cases}}{\text{the population at risk}} \times 100{,}000.$$

Incidence rate from confirmed invasive Salmonella infections were estimated using Adjusted incidence rates (AIRs) per 100,000 PYO in the catchment population. Calculated PYO in catchment area was by projecting the study population from the start to the end of recruitment period using annual growth rates of the country.

Assumptions in the calculation of S. Typhi in Burkina Faso Some assumptions were made to calculate incidence rate of S. Typhi in participants who were enrolled in the study. The first assumption was that the blood culture sensitivity test was only 50 % sensitive meaning that 50% of positive cases were missed during testing. The second assumption was that just 50% of the eligible population was enrolled due to limited capacity for enrollment. For those participants who either sick but with low temperatures were excluded and even those sick but not living in the catchment area were equally excluded from the study.

This number of positive cases were augmented considering that all participants who were sick and seeking healthcare services were enrolled in the study with their blood samples collected for culture test. Another consideration was that participants who took auto medications before visiting the health structure will not have any influence on the blood culture sensitivity test due to pre-medication with antibiotics results in lower sensitivity of blood culture.

We used same age group range from Mark et al 2017 which is the range mostly used IVI.

RESULTS

During the one-year period of this study, 1,306 participants were enrolled from the catchment area. The results are presented in tables and figures with records showing more recruitment of women, 740/1,304 (56.74%) compared to men. Information on sex was unavailable for two participants. The most represented age group was children below 5 years of age 426/1,306 (32.62%) followed by aged 6-15 years old 285/1,306 (21.82%)

Table 1: Distribution of participants who consulted with symptoms by Age range

Age range (years)	Frequency	Percentage (%)
< 2	203	15.54
2-5	223	17.08
6-15	285	21.82
16-25	260	19.91
26-35	211	16.15
>36	124	9.49
Total	**1,306**	100.00

The most frequent symptoms in addition to fever on presentation were headache (703/1,306) participants, abdominal pain (440/1,306) participants, and vomiting (336/1,304) participants.

Table 2: Presenting Symptoms of patients during consultation by age range

Symptoms	Less than 2 years	2-5 years	6-15 years	16-25years	26 years and above	Total	
						Frequency.	Percentage (%)
Abdominal pain	14	82	110	139	95	440	33.69
Headache	14	66	200	262	161	703	53.83
Constipation	1	2	4	13	7	27	2.10
Vomiting	11	70	105	98	52	336	25.72
Diarrhea	14	72	15	31	15	147	11.25
Cough	17	104	35	32	25	213	16.31
Sore throat	0	1	4	8	6	19	1.45
Running nose	15	73	31	32	20	171	13.10
Rash	2	8	5	6	1	22	1.68
Total	**88**	**478**	**509**	**621**	**382**	**2,078**	**100.00**

Auto medication at home is a growing phenomenon in most underdeveloped countries due to lack of finances to obtain proper medical attention. Out of 1,306 participants enrolled 721 took pre-medication and 75 of then used antibiotics and the most commonly used antibiotics was Cotrimoxazole 24/75 participants recorded. This high used of Cotrimoxazole could be due to it cheap and readily available or because of its nature to treat bacterial infection and malaria parasite together. Another highly consumed drug was penicillin with 23/75 participants. On the other hand, oral cephalosporins was used by 1 participant at home which is a third line drug reserve for treatment in case of drug resistance. Tetracycline was also used by1 participant as auto medication which is a broad-spectrum antibiotic. In general, 75 participants used antibiotics before consulting and 3 of those participants took more than one type of antibiotic.

Analgesics recorded a similar number of consumptions (721) at home by participants and this was common within the under 5 years of age (271/721) participants before seeking medical attention. More participants (721) took analgesics against those who took antibiotics (72) which could also serve as an exclusion criterial for recruitment of participants.

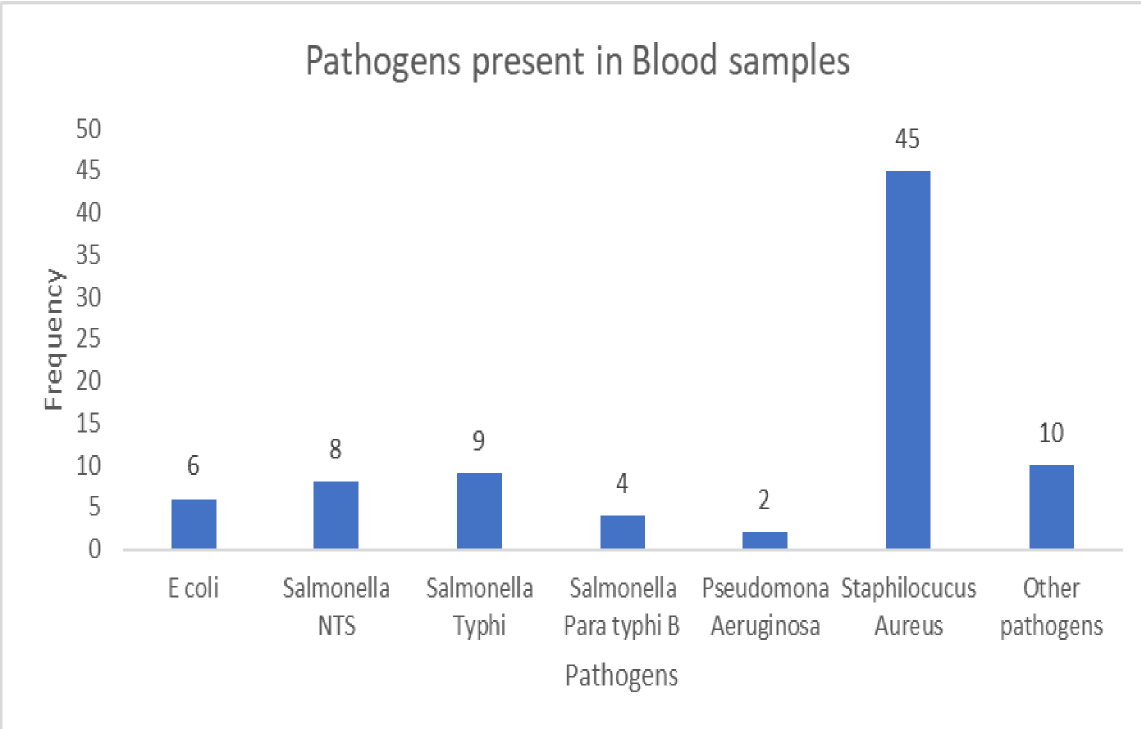
Table 3: Reported antibiotic and analgesic use from 75 participants reporting usage prior to the visit of health units;

Drugs		<2 years	2-5 years	6-15 years	16-25 years	26-35 years	>36 years	Total
Antibiotic	**Total**	**15**	**15**	**13**	**8**	**17**	**7**	**75**
	Penicillin	**4**	**4**	**5**	**4**	**4**	**2**	**23**
	Oral cephalosporins	**0**	**1**	**0**	**0**	**0**	**0**	**1**
	Erythromycin	**1**	**0**	**0**	**0**	**0**	**2**	**3**
	Doxycycline (Tetracycline)	**0**	**1**	**0**	**0**	**0**	**0**	**1**
	Ciprofloxacin	**0**	**1**	**0**	**0**	**6**	**1**	**8**
	Metronidazole	**3**	**2**	**2**	**1**	**4**	**0**	**12**
	Cotrimoxazole	**7**	**5**	**5**	**3**	**3**	**1**	**24**
	Others	**0**	**1**	**1**	**0**	**0**	**1**	**3**
Analgesics	**Total**	**120**	**151**	**177**	**126**	**87**	**45**	**721**

4.2. Laboratory results

This result was obtained from 1306 blood cultures performed between 16 June 2015 to 25 April 2016 in the laboratory and were classified into two categories; pathogens and contaminants. 84 pathogens were found positive in blood samples cultured with Staphylococcus Aureus 45/84 leading the positive number which is the causative bacteria for sore throat, and this was be reflected in children less than 5 years of age with 25 out of 45 Staphylococcus Aureus found in blood culture. The next pathogen with a high number was S. Typhi recording 9/84 positive blood cultured samples. Out of the 9 positive samples for TF, 3 positive cases were from the age range 6-15 years and 2 of those positives were from children under 5 years of age.

Figure 1: The different pathogens recorded in blood samples of participants



The 9 positive cases of S. Typhi isolates cultured from the blood samples of 1,306 febrile participants were used to calculate the incidence rate of S. Typhi in the catchment area.

Incidence = number of new cases divided by the population at risk over a time period of one year. **(9/28,701x100,000=31people**).

Table 4: Adjusted incidence rate for S. Typhi

	Population	PYO	Cases	Crude incidence rate (per 100,000 PYO)	Adjusted* incidence rate (per 100,000 PYO)
All ages	**1,306**	**28,701**	**9**	**31.35**	**125.43**
<2 years	**203**	**4,462**	**1**	**22.41**	**89.64**
2-5 years	**223**	**4,900**	**1**	**20.41**	**81.63**
6-15 years	**285**	**6,263**	**3**	**47.90**	**191.00**
16-25 years	**260**	**5,714**	**2**	**35.00**	**140.00**
26-35 years	**211**	**4,636**	**2**	**43.14**	**172.56**
>36 years	**124**	**2,726**	**0**	**0.00**	**0.00**

This result indicates that for every 100,000 people per year of observation 31 of them are affected with typhoid fever. Taking the assumptions in consideration, were blood culture test is 50% efficient, then 50% of positive results are missed. So 2x9 positive cases for S. Typhi =18.

With the other assumption of just 50% of population consulted and had 18 positive cases, and if 100% of participants are enrolled in the study, then the positive case will be 2x18= 36.

For the incidence will be = 36/28,701 x 100,000

=**125per 100,000 person-year of observation**. The method used to calculation of the AIR for the total number of cases apply to all the different age ranges.

For every 100,000 persons in the community 125 persons are affected with the typhoid fever.

Coagulase negative Staphylococci (CNS) was the most prevalent contaminant 122/173. This CNS contaminant is well known for negative influence on bacterial in the blood stream.

Table 5: Bacteria and contaminants identified in blood samples of participants during Laboratory testing.

		<2 years	2-5 years	6-15 years	16-25 years	26-35 years	>36 years	Total
Pathogens	Total	**24**	**18**	**15**	**10**	**11**	**6**	**84**
	E coli	**1**	**1**	**0**	**0**	**2**	**2**	**6**
	Non-Tyhpoid Salmonella	**3**	**2**	**0**	**0**	**3**	**0**	**8**
	Salmonella Typhi	**1**	**1**	**3**	**2**	**2**	**0**	**9**
	Salmonella Para typhi B	**2**	**1**	**0**	**1**	**0**	**0**	**4**
	Pseudomonas Aeruginosa	**0**	**0**	**1**	**1**	**0**	**0**	**2**
	Staphylococcus Aureus	**14**	**12**	**11**	**5**	**1**	**3**	**45**
	Other pathogens	**3**	**2**	**0**	**1**	**3**	**1**	**10**
Contaminants	Total	**50**	**39**	**33**	**13**	**17**	**21**	**173**
	Bacillus	**8**	**5**	**15**	**4**	**7**	**11**	**50**
	CNS	**42**	**34**	**17**	**9**	**10**	**10**	**122**
	Viridians Streptococci	**0**	**0**	**1**	**0**	**0**	**0**	**1**

Multi-drug resistance was defined as bacteria resistance to 3 or more different classes of antibiotics. From Table 6 shows the occurrence of MDR S. Typhi isolates to three groups of antibiotics; the beta-lactams (Penicillin and Amoxicillin) class, antihistamines (Chloramphenicol) class and sulfonamides (Cotrimoxazole) class of antibiotics. In more detail, a total of 7 S. Typhi isolates were resistant to three different classes of antibiotics, 3 isolates of Salmonella Typhi were resistant to Cotrimoxazole, while 3 other Salmonella Typhi isolates were resistant to the Penicillin's and Amoxicillin, while 1 isolate of S. Typhi was resistant to Chloramphenicol.

Another bacterium that had resistance was E. coli with 4 isolates resistant to Cotrimoxazole. Other pathogens like; 5 Salmonellae (NTS) isolates, 14 Staphylococcus Aureus isolates, 2 Salmonella Para typhi B isolates, and 3 S. Typhi isolates were all resistant to Cotrimoxazole. Staphylococcus Aureus isolates were the only isolates that had resistant to all the different types of antibiotics and almost all the pathogens isolated had resistant to Cotrimoxazole.

Table 6: Antimicrobial profile of isolated bacteria resistance to antibiotics.

Drug	Amoxicillin	Ceftazidime	Cefuroxime	Chloramphenicol	Cotrimoxazole	Penicillin
E. coli	**4/8**	**1/8**	**2/8**	**0**	**4/8**	**2/8**
Salmonellae (NTS)	**3/8**	**0**	**0**	**3/8**	**5/8**	**2/8**
Salmonella Typhi	**1/9**	**0**	**0**	**1/9**	**3/9**	**2/9**
Salmonella Paratyphi B	**1/4**	**1/4**	**0**	**1/4**	**2/4**	**1/4**
Pseudomonas aeruginosa	**1/2**	**0**	**0**	**1/2**	**0**	**0**
Staphylococcus Aureus	**5/46**	**2/46**	**4/46**	**6/46**	**14/46**	**6/46**
Other	**2/11**	**0**	**0**	**0**	**0**	**5/11**

The results of blood test using the malarial rapid test for 1,306 participants, recorded 576 positive malaria parasites in 1300 blood samples approximately 44.3%, indicative of high malaria prevalence in the catchment area as seen on Table 6. Results from 6 blood samples were not recorded due to missing registration information.

Table 7: Malaria test results for patients that consulted with fever.

Malaria	Frequency	Relative Frequency
Positive	576	44.3%
Negative	724	55.7%
total	1,300	100.0%

DISCUSSION

S. Typhi was identified as the primary cause of invasive bacterial infection higher among children under the ages of 15 years old with a total score of 5/9 positive samples and 2 of these positives were in children less than 5 years old in Nioko and Polesgo catchment area in Ouagadougou, Burkina Faso. Results from previous studies suggest that Typhoid fever in some sub-Saharan Africa settings occurs predominately in urban settlements with high-population densities, and that disease incidence could have been overestimated using the Widal test(Balasubramanian et al., 2018). This study was carried out in a semi urban setting which indicated a high incidence of Typhoid fever in areas with high-population densities.

The results of this study show that 125 cases per 100,000 PYO is higher than the estimated burden of S. Typhi infection in Africa which affect mostly children under the ages of 15 years in Ouagadougou, Burkina Faso. These estimates were not valid to my opinion because comparing two estimates from two different studies is difficult to have a correct estimate due to many factors put in place by Marks et al., with same protocol and in same site which does not match each other. The method used in those studies to calculate the population were different which will give different results at the end but to prevent this high incidence of typhoid fever the population need good access to safe drinking water and improved sanitation as well as effective treatment options of S. Typhi infection. The use of new TF conjugate vaccines for immunization against TF might provide more powerful tools for disease control.

E coli and Staphylococcus aureus were also most frequent non-Salmonella pathogens isolated from blood culture of participants. Malaria prevalence was also high in the catchment area that double the nature and burden of disease affecting the under 15 years of age with the impact more on the under 5years old.

Results of this study also identified a high prevalence of resistance against first-line antimicrobials in S Typhi infections as seen on Table 6. Cotrimoxazole and Penicillin were the drugs that recorded high prevalence of resistance by the S. Typhi and these same drugs also recorded a high consumption as premedication at home by the participants due to the availability, cheap and their broad-spectrum nature to treat bacterial infection.

Doing a study in the catchment area had some motivating factors such as; a well-established laboratory and qualified microbiology technical staff to do a reliable and quality blood culture test which will make the results of the study more reliable. The geographical location and accessibility of the health structure greatly influences all types of participants to seek for health interventions thereby increasing the number of participants who are eligible for enrollment into the study. This study enrolled a small population size for convenient in order to achieve quality and reliable results thereby gaining time.

The use of a blood culture test in the laboratory to diagnose TF was a motivating factor for good results because it is the most reliable test to diagnose Typhoid than those that were using Widal test to diagnose Typhoid.

With the motivating factors that had great positive influence to this study, there were equally some limitations to this study that had a negative feedback being that majority of the blood isolate tests for drugs resistance were Not performed which could give a much better result of drug resistance in the catchment area. This led to under reporting of the prevalence of drug resistance in the study site.

Using blood culture as the most reliable test to diagnose typhoid fever was not 100% efficient implying that 50% of the number of positive cases were missed thereby under reporting the prevalence and incidence of the disease.

The study time was limited to about one year which cannot reflect longer epidemiological trends. Auto medication by some participants also play a greater role to reduce blood culture sensitivity thereby masking the disease and excluding some participant whose temperatures were low during the time of enrollment. All these poor diagnoses and auto medication could lead to misused of drugs thereby leading to drug resistant which is global treat.

This study was carried out in a small area having a small population which did not cover the whole region leading to few numbers of cases from the community resulting to false incidence of Typhoid fever. The population used was an estimated population from marks et al in 2017 because that same site is also involved in the HDSS. This estimated population greatly influence the results positively by increasing the incidence of typhoid fever in Burkina Faso.

Strengthen

The study site had a well-established laboratory and qualified microbiology technical staff to perform blood culture.

The study population was well described due to enrollment in a health and demographic surveillance system (HDSS)

Weakness

Blood culture sensitivity test was assumed to be 50% sensitive giving rise to underestimation of typhoid fever cases.

We did very simple calculations for the AIR that did not account for 95% confidence interval thereby giving uncertainty in the calculations.

The study time was limited to one year which make it unable to detect long-term trends. Pre-treatment also by patients results in reduced blood culture sensitivity.

CONCLUSION

S. Typhi bacteria is a bloodstream infection found mostly in children below 15 years of age with a greater impact felt in the under 5 years old children in Ouagadougou, Burkina Faso. This age group is considered by WHO as a risky population. Results from Marks et. al 2017 study have shown that Typhoid fever vaccine in highly effective in affected areas and will greatly reduce the bacteria incidence of typhoid fever in the catchment area. Other studies hold that improved sanitation, safe drinking water as well as effective treatment options of S. Typhi infection will greatly reduce the spread of the disease.

Considering the assumptions and weaknesses of this study in the estimation of incidence rate of Typhoid fever in Ouagadougou we might give contradicting incidence of S. Typhi which is not real situation of the disease so; further studies in additional sites and different settings are required in order to generate evidence supporting a national campaign with typhoid conjugate vaccine, information on severity, including mortality due to typhoid is needed.

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